

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
18 August 2005 (18.08.2005)

PCT

(10) International Publication Number
WO 2005/075717 A1

(51) International Patent Classification⁷: **C30B 30/00**

(21) International Application Number:
PCT/CA2005/000158

(22) International Filing Date: 9 February 2005 (09.02.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/542,294 9 February 2004 (09.02.2004) US

(71) Applicant (for all designated States except US): **SIMON FRASER UNIVERSITY** [CA/CA]; Room 2100, Strand Hall, Industry Liaison Office, Burnaby, British Columbia V5A 1S6 (CA).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **AGNES, George, R.** [CA/CA]; 2387 Huron Drive, Coquitlam, British Columbia V3J 6Y7 (CA). **BOGAN, Michael, J.** [CA/CA]; Suite 901, 9521 Cardston Court, Burnaby, British Columbia V3N 4R9 (CA). **BAKHOUM, Samuel, F.W.** [CA/CA]; Room 3150 Strand Hall, c/o Simon Fraser University/Industry Liaison Office, Burnaby, British Columbia V5A 1S6 (CA).

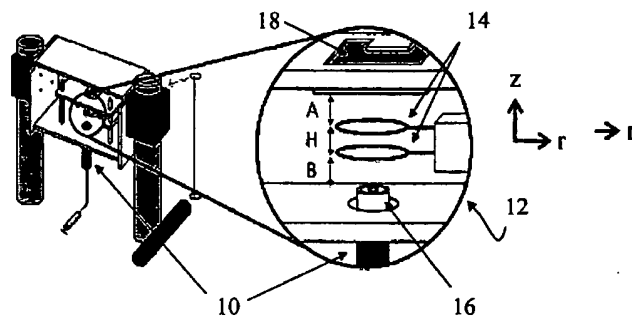
(74) Agents: **BAILEY, Thomas, W.** et al.; Suite 480 - The Station, 601 West Cordova Street, Vancouver, British Columbia V6B 1G1 (CA).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

[Continued on next page]

(54) Title: CONTROLLED NUCLEATION OF SOLUTES IN SOLUTIONS HAVING NET CHARGE TO PROMOTE CRYSTAL GROWTH



(57) Abstract: This application is concerned with the controlled nucleation of solutes (i.e. dissolved solids) from solution. It has been found that the energy barrier for dissolved solids to nucleate is affected by the surface charge density of the reaction vessel (and hence the mass-to-charge ratio of vessel). The reaction vessel may, for example, comprise a levitated droplet of the solution having an "excess net charge". That is, ions present in the vessel of a single polarity are in excess of the counterions of opposite polarity. An increase in the surface charge density of the vessel (and hence a reduction in the mass-to-charge ratio of the vessel) causes the barrier for nucleation to decrease. These findings can be exploited using instruments commonly used in wall-less sample preparation to elicit selective control over the induction of nucleation and subsequent crystallization of target solutes of interest in the condensed phase. The ion induced nucleation phenomenon, in reaction vessels having a desirable surface charge density, is likely to be general for all dissolved solids, ranging from inorganic compounds, to low and high molecular weight organic compounds, including proteins and other molecules. For example the present invention can be used to selectively crystallize a target solute or to separate different solutes from one another based on their propensity to nucleate at different reaction conditions. The different solutes could constitute different compounds or different stereochemical forms of same compound. The invention could also be exploited to controllably select or separate polymorphic forms of a compound (which may often have very different biological activity). The crystals derived from the process could be the subject of further analysis, characterization or manipulation, for example as a prepared sample for MALDI-TOF MS.

WO 2005/075717 A1



Published:

— with international search report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.